

-continued

(i i) MOLECULE TYPE: DNA (genomic)

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:4:

CATCTGAACT CAAAGCGTGG

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What is claimed is:

1. A method of killing a tumor cell in a patient in need thereof, comprising directly administering to said tumor cell therapeutically effective amounts of a viral vector and a DNA damaging agent, wherein said viral vector comprises a DNA sequec encoding p53 operatively linked to a promoter, and wherein expression of said p53 and DNA damage result in the killing of said tumor cell.

2. The method of claim 1, wherein said viral vector is selected from the group consisting of retrovirus, adenovirus, herpesvirus, adeno-associated virus and cytomegalovirus.

3. The method claim 2, wherein the tumor cell is contacted with a pharmaceutical composition comprising a DNA damaging compound.

4. The method of claim 3, wherein the DNA damaging agent is cisplatin.

5. The method of claim 4, wherein said cisplatin is administered at 20 mg/m².

6. The method of claim 3, wherein the DNA damaging agent is doxorubicin.

7. The method of claim 6, wherein said doxorubicin is administered at 25-75 mg/m².

8. The method of claim 3, wherein the DNA damaging agent is etoposide.

9. The method of claim 8, wherein said etoposide is administered at 35-50 mg/m².

10. The method of claim 3, wherein the DNA damaging agent is verapamil.

11. The method of claim 3, wherein the DNA damaging agent is podophyllotoxin.

12. The method of claim 3, wherein the DNA damaging agent is 5-FU.

13. The method of claim 12, wherein said 5-FU is administered at 3-15 mg/kg.

14. The method of claim 2, wherein said viral vector is a retroviral vector.

15. The method of claim 2, wherein said viral vector is an adenoviral vector.

16. The method of claim 15, wherein the amount of adenoviral vector is 1×10^5 to 1×10^{12} pfu.

17. The method of claim 16, wherein said amount is 5×10^7 pfu.

18. The method of claim 16, wherein said amount is 2×10^7 pfu.

19. The method of claim 2, wherein said viral vector is a herpesviral vector.

20. The method of claim 2, wherein said viral vector is an adeno-associated viral vector.

21. The method of claim 2, wherein said viral vector is a cytomegaloviral vector.

22. The method of claim 1, wherein said promoter is a constitutives promoter.

23. The method of claim 22, wherein the promoter is selected from the group consisting of SV40, CMV and RSV.

24. The method of claim 23, wherein the promoter is the CMV IE promoter.

25. The method of claim 24, wherein the viral vector further comprises a polyadenylation signal.

26. The method of claim 25, wherein the viral vector is an adenoviral vector.

27. The method of claim 1, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with X-ray radiation, UV-irradiation, γ -irradiation or microwaves.

28. The method of claim 27, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with X-ray radiation.

29. The method of claim 28, wherein the x-ray dosage is between 2000 and 6000 roentgens.

30. The method of claim 28, wherein the x-ray -dosage is between 50 and 200 roentgens.

31. The method of claim 27, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with UV-irradiation.

32. The method of claim 27, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with γ -irradiation.

33. The method of claim 27, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with microwaves.

34. The method claim 1, wherein the tumor cell is contacted with a DNA damaging agent by administering to the patient a pharmaceutical composition comprising a DNA damaging compound.

35. The method of claim 1, wherein said viral vector is administered prior to said DNA damaging agent.

36. The method of claim 1, wherein said viral vector is administered after said DNA damaging agent.

37. The method of claim 1, wherein said viral vector is administered at the same time as said DNA damaging agent.

38. The method of claim 1, wherein said viral vector is delivered endoscopically, intravenously, intratracheally, intralesionally, percutaneously or subcutaneously.

39. The method of claim 1, wherein said tumor is located in a resected tumor bed.

40. The method of claim 1, wherein said administering is repeated.

41. The method of claim 1, wherein said tumor cell is a lung cancer cell.

42. The method of claim 41, wherein said lung cancer cell is non-small cell lung carcinoma cell.

43. The method of claim 42, wherein said non-small cell lung carcinoma cell is a squamous carcinoma cell.

44. The method of claim 42, wherein said non-small cell lung carcinoma cell is an adenocarcinoma cell.

45. The method of claim 42, wherein said non-small cell lung carcinoma cell is a large-cell undifferentiated carcinoma cell.

46. The method of claim 41, wherein said lung cancer cell is a small cell lung carcinoma cell.

47. The method of claim 1, wherein said tumor cell is an epithelial tumor cell.

48. The method of claim 1, wherein said tumor cell is a breast cancer cell.

49. The method of claim 1, wherein said viral vector is administered in about 0.1 ml.

50. The method of claim 1, wherein said viral vector is administered in about 10 ml.

51. A method of treating cancer in a cancer patient, comprising directly administering to a tumor site therapeutically effective amounts of a viral vector and a DNA damaging agent, wherein said viral vector comprises a DNA sequence encoding p53 operatively linked to a promoter, and wherein expression of said p53 and DNA damage result in treatment of said cancer.

52. The method of claim 51, wherein said viral vector is selected from the group consisting of retrovirus, adenovirus, herpesvirus, adeno-associated virus and cytomegalovirus.

53. The method of claim 52, wherein said viral vector is a retroviral vector.

54. The method of claim 52, wherein said viral vector is an adenoviral vector.

55. The method of claim 54, wherein the amount of adenoviral vector is 1×10^5 to 1×10^{12} pfu.

56. The method of claim 55, wherein said amount is 5×10^7 pfu.

57. The method of claim 55, wherein said amount is 2×10^7 pfu.

58. The method of claim 52, wherein said viral vector is a herpesviral vector.

59. The method of claim 52, wherein said viral vector is an adeno-associated viral vector.

60. The method of claim 52, wherein said viral vector is a cytomegaloviral vector.

61. The method of claim 51, wherein the tumor site is contacted with a DNA damaging agent by irradiating the tumor site with X-ray radiation, UV-irradiation, γ -irradiation or microwaves.

62. The method of claim 61, wherein the tumor site is contacted with a DNA damaging agent by irradiating the tumor site with X-ray radiation.

63. The method of claim 62, wherein the x-ray dosage is between 2000 and 6000 roentgens.

64. The method of claim 62, wherein the x-ray dosage is between 50 and 200 roentgens.

65. The method of claim 61, wherein the tumor site is contacted with a DNA damaging agent by irradiating the tumor site with UV-irradiation.

66. The method of claim 61, wherein the tumor site is contacted with a DNA damaging agent by irradiating the tumor site with γ -irradiation.

67. The method of claim 61, wherein the tumor site is contacted with a DNA damaging agent by irradiating the tumor site with microwaves.

68. The method claim 51, wherein the tumor site is contacted with a DNA damaging agent by administering to the patient a pharmaceutical composition comprising a DNA damaging compound.

69. The method of claim 68, wherein the DNA damaging compound is cisplatin.

70. The method of claim 69, wherein said cisplatin is administered at 20 mg/m^2 .

71. The method of claim 68, wherein the DNA damaging agent is doxorubicin.

72. The method of claim 71, wherein said etoposide is administered at $35\text{--}50 \text{ mg/m}^2$.

73. The method of claim 72, wherein said doxorubicin is administered at $25\text{--}75 \text{ mg/m}^2$.

74. The method of claim 68, wherein the DNA damaging agent is etoposide.

75. The method of claim 68, wherein the DNA damaging agent is verapamil.

76. The method of claim 68, wherein the DNA damaging agent is podophyllotoxin.

77. The method of claim 68, wherein the DNA damaging agent is 5-FU.

78. The method of claim 77, wherein said 5-FU is administered at $3\text{--}15 \text{ mg/kg}$.

79. The method of claim 51, wherein said viral vector is administered prior to said DNA damaging agent.

80. The method of claim 79, wherein the period between administration of the viral vector and DNA damaging agent is between 12 and 24 hours.

81. The method of claim 79, wherein the period between administration of the viral vector and DNA damaging agent is between 6 and 12 hours.

82. The method of claim 79, wherein the period between administration of the viral vector and DNA damaging agent is about 12 hours.

83. The method of claim 51, wherein said viral vector is administered after said DNA damaging agent.

84. The method of claim 83, wherein the period between administration of the DNA damaging agent and viral vector is between 12 and 24 hours.

85. The method of claim 83, wherein the period between administration of the DNA damaging agent and viral vector is between 6 and 12 hours.

86. The method of claim 83, wherein the period between administration of the DNA damaging agent and viral vector is about 12 hours.

87. The method of claim 51, wherein said viral vector is administered at the same time as said DNA damaging agent.

88. The method of claim 51, wherein said viral vector is delivered endoscopically, intravenously, intratracheally, intralesionally, percutaneously or subcutaneously.

89. The method of claim 51, wherein said tumor site is a resected tumor bed.

90. The method of claim 51, wherein said administration is repeated.

91. The method of claim 51, wherein said cancer is a lung cancer.

92. The method of claim 91, wherein said lung cancer is a non-small cell lung carcinoma cancer.

93. The method of claim 92, wherein said non-small cell lung carcinoma cancer is a squamous carcinoma cancer.

94. The method of claim 92, wherein said non-small cell lung carcinoma cancer is an adenocarcinoma cancer.

95. The method of claim 92, wherein said non-small cell lung carcinoma cancer is a large-cell undifferentiated carcinoma cancer.

96. The method of claim 91, wherein said lung cancer is a small cell lung carcinoma cancer.

97. The method of claim 51, wherein said cancer is an epithelial cancer.

98. The method of claim 51, wherein said cancer is breast cancer.

99. The method of claim 51, wherein said viral vector is administered in about 0.1 ml.

100. The method of claim 51, wherein said viral vector is administered in about 10 ml.

101. The method of claim 2, wherein said promoter is a constitutive promoter.

102. The method of claim 101, wherein said promoter is selected from the group consisting of SV40, CMV and RSV.

103. The method of claim 102, wherein the promoter is the CMV IE promoter.

104. The method of claim 103, wherein the viral vector further comprises a polyadenylation signal.

105. The method of claim 104, wherein the viral vector is an adenoviral vector.

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